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PRINCIPAL INVESTIGATOR: Paul Zalzal

CONTRACTING ORGANIZATION: McMaster University
Hamilton, Ontario

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6. AUTHOR(S) Dr. Paul Zalzal Associates: Ehsan Toyserkani; Hurtig Marc; Grynpas Michael; Mark McKee Marilyn Boitano; Robert Pilliar; Rita Kandel E-Mail: paulzalzal@gmail.com			7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) McMaster University Hamilton, Ontario	
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14. ABSTRACT Currently amputation, arthrodesis (joint fusion), or joint replacement are used to treat a joint with an intra-articular fracture or destroyed by a combat injury. Generation of personalized, anatomically shaped biological implants formed using techniques of regenerative medicine in conjunction with biodegradable biomaterial structures to restore a damaged articular joint surface to normal tissue structure, form and function is one way to overcome the limitations associated with current treatment methods. The <i>aims of this study</i> are to: 1) identify the parameters that generate anatomically shaped bone substitutes of optimal composition and structure with an articulating profile. 2) to develop a source of chondrocytes that can generate sufficient amounts of a cartilage layer to cover the bone substitute; and 3) to evaluate the structures formed in a preclinical model. The ongoing studies will further our understanding of the regulation of cell differentiation to chondrocytes and the bone substitute properties required to form a biological joint replacement.				
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Table of Contents

	Page
INTRODUCTION	2
KEYWORDS:	3
OVERALL PROJECT SUMMARY	see Kandel Final Report (W81XWH-10-1-0787)
KEY RESEARCH ACCOMPLISHMENTS	see Kandel Final Report (W81XWH-10-1-0787)
CONCLUSION	see Kandel Final Report (W81XWH-10-1-0787)
PUBLICATIONS, ABSTRACTS, AND PRESENTATIONS	see Kandel Final Report (W81XWH-10-1-0787)
INVENTIONS, PATENTS AND LICENSES	see Kandel Final Report (W81XWH-10-1-0787)
REPORTABLE OUTCOMES	see Kandel Final Report (W81XWH-10-1-0787)
OTHER ACHIEVEMENTS	see Kandel Final Report (W81XWH-10-1-0787)
REFERENCES	see Kandel Final Report (W81XWH-10-1-0787)
APPENDICES	see Kandel Final Report (W81XWH-10-1-0787)

INTRODUCTION

The complexity of extremity injuries as a consequence of battlefield trauma requires multifaceted reconstructions and has resulted in the need to develop entirely new treatment options to achieve limb salvage and thus full rehabilitation. **The overall aim of this research project was to develop large anatomically shaped biological implants formed using techniques of regenerative medicine in conjunction with biodegradable biomaterial structures to restore a damaged articular joint surface to normal tissue structure, form and function. The surgical methods to evaluate these implants in a pre-clinical sheep model was developed.** Our multi-disciplinary team was focused on generating medial tibial plateau and a large segment of the medial femoral condyle (knee joint) biphasic implants (definitive care of battle injuries). The approach we developed has resulted in an implant that can be customized contoured to replace the portion of the knee joint disrupted either by an intra-articular fracture or trauma. Being able to generate personalized implants is a critical feature given that most combat injuries are irregularly shaped.

Using an approach that allows for the formation of living tissues for joint reconstruction offers the advantage of functional tissue integration as well as adaptation to loading conditions during use which should avoid implant failure that can result from the fatigue or wear of synthetic biomaterial. This approach allows the generation of an implant of any contour, making this approach particularly appropriate for individuals who have irregular-shaped defects as a result of a combat injury. Three issues had to be overcome before these large biphasic constructs can be

used clinically, particularly in the military setting, are 1) the identification of an accessible human cell source to generate a large quantity of cartilage tissue; 2) the methodology to easily, rapidly and reliably generate custom-made CPP bone substitutes of desired shape; 3) develop a pre-clinical animal model to evaluate these implants. This report will summarize the results obtained during this grant period.

As my portion of the project is intertwined and interdependent with all aspects of this research, my final report would be identical to Dr. Rita Kandel (Toronto, Ontario, Canada). For this reason we have submitted only one final report. Please refer to her report for information.

KEYWORDS:

Joint restoration, cartilage tissue engineering, bone substitute biomaterial, cartilage repair